Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

REVIEW

Waon Therapy for Cardiovascular Disease
– Innovative Therapy for the 21st Century –

Masaaki Miyata, MD; Chuwa Tei, MD

Waon therapy is a form of thermal treatment in a dry sauna maintained at a temperature of 60°C, which differs from the traditional sauna. Waon therapy reportedly improves the hemodynamics, cardiac function, ventricular arrhythmias, vascular endothelial function, neurohormonal factors, sympathetic nervous system function, and symptoms in patients with chronic heart failure (CHF). It has also been demonstrated that the molecular mechanism by which Waon therapy improves vascular flow and endothelial function involves increased expression of endothelial nitric oxide synthase (eNOS). Furthermore, in a mouse model of hindlimb ischemia, repeated Waon therapy increased eNOS protein expression, blood flow, and capillary density. Moreover, Waon therapy did not increase blood flow and capillary density in eNOS-deficient mice, indicating that eNOS is a critical regulator of the angiogenesis induced by this therapy. Moreover, repeated Waon therapy is effective for patients with severe peripheral arterial disease (PAD), as evidenced by substantial decrease in pain scores, increases in both ankle–brachial pressure index and blood flow assessed by laser Doppler perfusion imaging, and by formation of new collateral vessels on angiography. In addition, ischemic ulcers heal or improve markedly. In conclusion, Waon therapy is an innovative and highly promising strategy for treating CHF and PAD. (*Circ J* 2010; **74:** 617–621)

Key Words: Chronic heart failure; Nitric oxide; Peripheral arterial disease; Waon therapy

In 1989 we developed a form of thermal therapy for heart failure that uses a dry sauna with temperature maintained at 60°C, which differs from the traditional sauna. In 2007, we changed the name to Waon therapy:[1] "Wa" means soothing, and "On" means warmth, hence Waon or "soothing warmth" infers a warmth that comfortably refreshes the mind and body. Waon therapy is defined as warming the entire body in a uniformly heated chamber for 15 min at a temperature that relaxes the mind and body. After the core temperature has increased by 1.0–1.2°C, the patient rests outside the sauna for a further 30 min to maintain the soothing effect, and fluids corresponding to perspiration are supplied to protect against dehydration at the end of therapy.

We discovered that this new thermal therapy offers substantial benefits for patients with cardiovascular diseases, including chronic heart failure (CHF)[2–8] and peripheral artery disease (PAD),[9,10] as well as lifestyle-related diseases.[11,12] In this review, we summarize the beneficial effects of Waon therapy on cardiovascular disease.

How to Perform Waon Therapy

Waon therapy requires a far-infrared-ray dry sauna, which is uniformly maintained at 60°C without hydration pressure. Patients remain in the dry sauna for 15 min, and then rest supine on a bed outside the sauna where they are covered with blankets for an additional 30 min (**Figure 1**). They are weighed before and after Waon therapy and drink water to compensate for weight loss by perspiration.

We have already used Waon therapy for many CHF patients, and none so far have shown any deterioration in their condition. However, Waon therapy does not appear to be indicated for CHF patients with severe aortic stenosis or severe obstructive hypertrophic cardiomyopathy because the treatment might increase the pressure gradient. Patients with active infectious disease and high fever are also excluded from Waon therapy.

Effect of Waon Therapy on CHF

CHF is a major and growing public health problem in Japan, as in other developed countries. Drugs that interfere with excessive activation of the renin–angiotensin–aldosterone system can relieve the symptoms of heart failure in patients with a reduced ejection fraction (EF) by stabilizing or reversing cardiac remodeling. Thus, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and β-blockers have emerged as cornerstones of modern heart failure therapy for patients with a depressed EF.[13–15] However, the number of deaths from heart failure has increased

Received December 1, 2009; revised manuscript received December 19, 2009; accepted December 21, 2009; released online February 13, 2010

Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, Kagoshima, Japan

Mailing address: Masaaki Miyata, MD, Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan. E-mail: miyatam@m3.kufm.kagoshima-u.ac.jp

ISSN-1346-9843 doi:10.1253/circj.CJ-09-0939

Figure 1. Waon therapy.

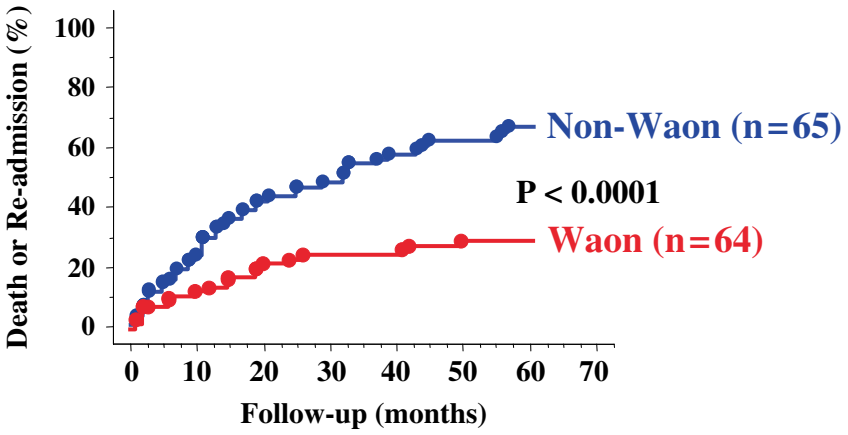

Figure 2. Effects of Waon therapy on prognosis of chronic heart failure patients. (Adapted and modified from Kihara et al.[8])

steadily despite advances in treatment, in part because of increasing numbers of patients with CHF as a result of earlier and better treatment of acute myocardial infarction.[16] Therefore, new therapies for CHF must be developed.

We developed Waon therapy for CHF and have been investigating its effects since 1989. Regarding the acute effects, we reported that taking a 60°C sauna for 15 min improved the hemodynamics in patients with CHF, including the cardiac index, mean pulmonary wedge pressure, systemic and pulmonary resistance, and cardiac function.[2] Subsequently, we examined the chronic effects of repeated Waon therapy on CHF and we have found that 4 weeks of Waon therapy significantly improved symptoms, increased the EF, and decreased the cardiac size on both the echocardiogram and chest X-ray.[2,3] Furthermore, we demonstrated that daily Waon therapy for 2 weeks decreased ventricular premature contractions and increased heart rate variability (standard deviation of normal-to-normal beat interval) in patients with CHF, suggesting that Waon therapy decreased sympathetic nervous activity and improved ventricular arrhythmias.[5] In a prospective multicenter study, we have confirmed that Waon therapy is safe, improves clinical symptoms and cardiac function, and decreases cardiac size in CHF patients.[6]

Recently, we assessed the impact of Waon therapy on the prognosis of 129 patients with CHF: 64 underwent Waon therapy, 65 did not, and the patients were followed for 5 years. The patients in the Waon group continued the therapy at least twice weekly after discharge. Waon therapy significantly decreased the rate of death or hospitalization in patients with CHF in comparison with the non-Waon therapy group (Figure 2).[8] This retrospective follow-up study demonstrated that Waon therapy reduced cardiac events related to heart failure over a 60-month period. We therefore recommend that Waon therapy should be continued at least twice weekly after discharge in order to maintain its effect on CHF.

Mechanism by Which Waon Therapy Improves CHF

There is a vicious cycle between heart failure and vascular failure. Patients with heart failure show decreased peripheral blood flow, decreased shear stress, decreased nitric oxide (NO) release from the endothelium, and vascular failure. As

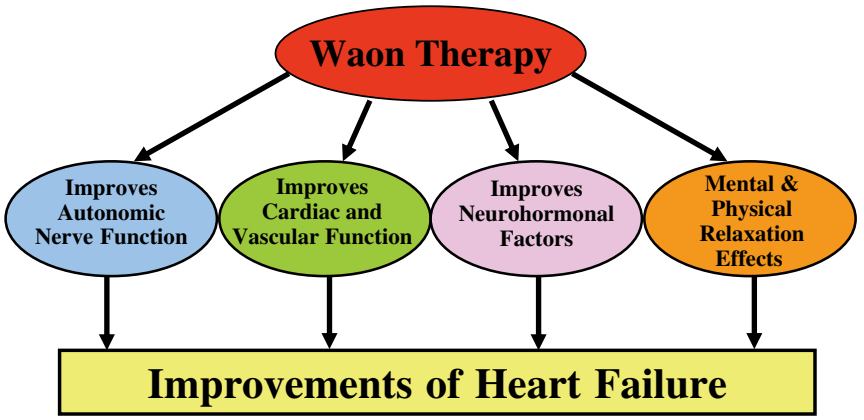

Figure 3. Pleiotropic effects of Waon therapy on chronic heart failure.

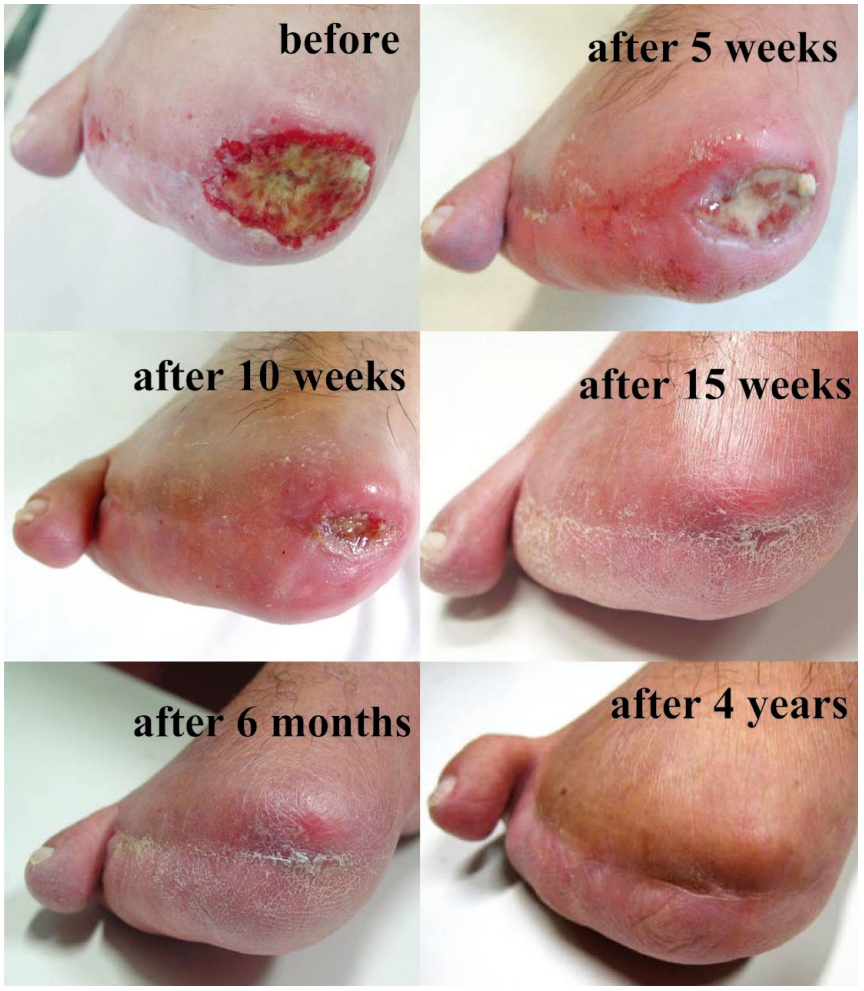

Figure 4. Healing of foot ulcer after Waon therapy. (Adapted and modified from Tei et al.[10])

a result, vascular endothelial function decreases, peripheral resistance increases, cardiac pre- and afterload increase, and heart failure worsens. We therefore investigated vascular endothelial function to clarify the mechanism of the effect of Waon therapy on CHF. We reported that 2 weeks of Waon therapy significantly reduced brain natriuretic peptide (BNP) concentrations and improved endothelial function in patients with CHF. There was a significant correlation between the percent change in flow-mediated dilatation and the percent improvement in BNP concentration.[4] This finding suggests that Waon therapy improves cardiac function in parallel with vascular function.

In order to confirm the effect of Waon therapy on CHF and clarify its mechanism, we performed experimental studies

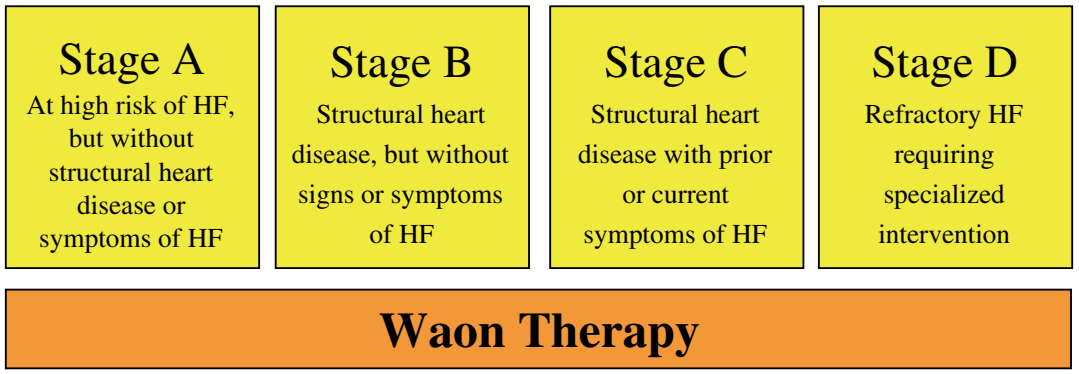

Figure 5. Proposed position of Waon therapy in management of chronic heart failure (HF).

using TO-2 cardiomyopathic hamsters with heart failure and found that repeated Waon therapy improved survival.[17] In other studies, we clarified that 1 of the molecular mechanisms by which repeated Waon therapy improved endothelial function was an increase in the mRNA and protein of endothelial NO synthase (eNOS) in both Syrian golden hamsters[18] and TO-2 cardiomyopathic hamsters.[19] We believe that eNOS upregulation induced by repeated Waon therapy is caused by an increase in cardiac output and blood flow, which in turn results in increased shear stress, although thermal stimulation might alternatively upregulate arterial eNOS directly. We are going to address the effects of Waon therapy on heat shock proteins, eNOS phosphorylation, and oxidative stress in vascular wall cells and cardiomyocytes in TO-2 cardiomyopathic hamsters.

In summary, Waon therapy improves cardiac and vascular functions, autonomic nerve function, and neurohormonal factors, while inducing mental and physical relaxation. These multiple effects thus ameliorate CHF (**Figure 3**).

Effect of Waon Therapy on PAD

We have shown that Waon therapy is safe for patients with severe PAD, and that Waon therapy for 10 weeks is potentially effective as evidenced by a substantial decrease in pain scores, increases in both the ankle–brachial pressure index and blood flow assessed by laser Doppler perfusion imaging, and by the formation of new collateral vessels on angiography. In addition, ischemic ulcers heal or improve markedly.[9,10]

We previously described a patient with an impressive result.[10] Although this patient had undergone femoropopliteal bypass surgery, the first 4 toes on his right foot had to be amputated. Furthermore, the patient developed a severe foot ulcer with intolerable pain. He underwent Waon therapy without any changes in medication. The skin ulcer healed completely in 15 weeks, limb amputation was avoided, and he was discharged. Thereafter, he continued to undergo Waon therapy twice weekly at the outpatient clinic and there has not been a recurrence of the skin ulcer during 4 years of follow-up (**Figure 4**).

Patients followed at the outpatient clinic after discharge continue Waon therapy at least twice weekly, and none have shown worsening symptoms of PAD. Therefore, to maintain the effect of Waon therapy, we believe that it should be continued at least twice weekly after discharge.

Mechanism by Which Waon Therapy Improves PAD

NO, constitutively produced by eNOS, plays a role in angiogenesis. Having reported that Waon therapy upregulates the expression of arterial eNOS in hamsters, we investigated whether this therapy increased angiogenesis in mice with hindlimb ischemia.[20] In a mouse model of hindlimb ischemia, we demonstrated that repeated Waon therapy increased eNOS protein expression, blood flow, and capillary density.

To study the possible involvement of eNOS in thermally induced angiogenesis, the mice underwent Waon therapy with and without administration of N^G-nitro-L-arginine methyl ester (L-NAME) for 5 weeks. L-NAME treatment abolished angiogenesis induced by Waon therapy. In addition, Waon therapy did not increase angiogenesis in eNOS-deficient mice. We conclude that eNOS is a critical regulator of the angiogenesis induced by Waon therapy.[20]

Effect of Waon Therapy on Lifestyle-Related Diseases

For patients with lifestyle-related diseases, Waon therapy for 2 weeks improves impaired vascular endothelial function in the setting of atherosclerotic risk factors, such as hypertension, hypercholesterolemia, diabetes mellitus, obesity, and smoking.[11] In addition, we investigated the effect of 2 weeks of Waon therapy on oxidative stress evaluated by urinary 8-epi-PGF2α levels in patients with at least 1 atherosclerotic risk factor. Urinary 8-epi-PGF2α levels were significantly decreased in the treated patients when compared with controls.[12] Thus, Waon therapy reduces oxidative stress and improves vascular function in patients with atherosclerosis risk factors.

Conclusion

Waon therapy is an innovative method of treating patients with CHF and so is not covered by existing guidelines. Waon therapy can be administered in stages A–D, and corresponds in position to ACE inhibitors and ARBs in the ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult[16] (**Figure 5**).

An ideal therapy in the 21st st century should be safe, free of side-effects, and have high medical value (ie, high benefit/

cost ratio). It should be non-invasive, and make patients feel better. Waon therapy fulfills all of these criteria and is therefore a promising therapy for patients with cardiovascular diseases such as CHF and PAD.

References

1. Tei C. Waon therapy: Soothing warmth therapy. *J Cardiol* 2007; **49:** 301–304.
2. Tei C, Horikiri Y, Park JC, Jeong JW, Chang KS, Toyama Y, et al. Acute hemodynamic improvement by thermal vasodilation in congestive heart failure. *Circulation* 1995; **91:** 2582–2590.
3. Tei C, Tanaka N. Thermal vasodilation as a treatment of congestive heart failure: A novel approach. *J Cardiol* 1996; **27:** 29–30.
4. Kihara T, Biro S, Imamura M, Yoshifuku S, Takasaki K, Ikeda Y, et al. Repeated thermal therapy treatment improves vascular endothelial and cardiac function in patients with chronic heart failure. *J Am Coll Cardiol* 2002; **39:** 754–759.
5. Kihara T, Biro S, Ikeda Y, Fukudome T, Shinsato T, Masuda A, et al. Effects of repeated sauna treatment on ventricular arrhythmias in patients with chronic heart failure. *Circ J* 2004; **68:** 1146–1151.
6. Miyata M, Kihara T, Kubozono T, Ikeda Y, Shinsato T, Izumi T, et al. Beneficial effects of Waon therapy on patients with chronic heart failure: Results of a prospective multicenter study. *J Cardiol* 2008; **52:** 79–85.
7. Basford JR, Oh JK, Allison TG, Sheffield CG, Manahan BG, Hodge DO, et al. Safety, acceptance, and physiologic effects of sauna bathing in people with chronic heart failure: A pilot report. *Arch Phys Med Rehab* 2009; **90:** 173–177.
8. Kihara T, Miyata M, Fukudome T, Ikeda Y, Shinsato T, Kubozono T, et al. Waon therapy improves the prognosis of patients with chronic heart failure. *J Cardiol* 2009; **53:** 214–218.
9. Tei C, Shinsato T, Miyata M, Kihara T, Hamasaki S. Waon therapy improves peripheral arterial disease. *J Am Coll Cardiol* 2007; **50:** 2169–2171.
10. Tei C, Shinsato T, Kihara T, Miyata M. Successful thermal therapy for end-stage peripheral artery disease. *J Cardiol* 2006; **47:** 163–164.
11. Imamura M, Biro S, Kihara T, Yoshifuku S, Takasaki K, Otsuji Y, et al. Repeated thermal therapy improves impaired vascular endothelial function in patients with coronary risk factors. *J Am Coll Cardiol* 2001; **38:** 1083–1088.
12. Masuda A, Miyata M, Kihara T, Minagoe S, Tei C. Repeated sauna therapy reduces urinary 8-epi-prostaglandin F(2alpha). *Jpn Heart J* 2004; **45:** 297–303.
13. Mann DL. Management of heart failure patients with reduced ejection fraction. *In*: Libby P, Bonow RO, Mann DL, Zipes DP, editors. Braunwald's heart disease: A textbook of cardiovascular medicine. 8th edn. Philadelphia: WB Saunders, 2008; 611–640.
14. Komukai K, Yagi H, Ogawa T, Date T, Morimoto S, Kawai M, et al. Inhibition of the renin-angiotensin system prevents re-hospitalization of heart failure patients with preserved ejection fraction. *Circ J* 2008; **72:** 2004–2008.
15. Miyagishima K, Hiramitsu S, Kimura H, Mori K, Ueda T, Kato S, et al. Long term prognosis of chronic heart failure: Reduced vs preserved left ventricular ejection fraction. *Circ J* 2009; **73:** 92–99.
16. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, et al; American College of Cardiology; American Heart Association Task Force on Practice Guidelines; American College of Chest Physicians; International Society for Heart and Lung Transplantation; Heart Rhythm Society. ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): Developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: Endorsed by the Heart Rhythm Society. *Circulation* 2005; **112:** e154–e235.
17. Ikeda Y, Biro S, Kamogawa Y, Yoshifuku S, Kihara T, Minagoe S, et al. Effect of repeated sauna therapy on survival in TO-2 cardiomyopathic hamsters with heart failure. *Am J Cardiol* 2002; **90:** 343–345.
18. Ikeda Y, Biro S, Kamogawa Y, Yoshifuku S, Eto H, Orihara K, et al. Repeated thermal therapy upregulates arterial endothelial nitric oxide synthase expression in Syrian golden hamsters. *Jpn Circ J* 2001; **65:** 434–438.
19. Ikeda Y, Biro S, Kamogawa Y, Yoshifuku S, Eto H, Orihara K, et al. Repeated sauna therapy increases arterial endothelial nitric oxide synthase expression and nitric oxide production in cardiomyopathic hamsters. *Circ J* 2005; **69:** 722–729.
20. Akasaki Y, Miyata M, Eto H, Shirasawa T, Hamada N, Ikeda Y, et al. Repeated thermal therapy up-regulates endothelial nitric oxide synthase and augments angiogenesis in a mouse model of hindlimb ischemia. *Circ J* 2006; **70:** 463–470.